BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 41 1208—1220 (1968)

Acid-Catalyzed Isomerization of 1,3,4,5-Tetra-*O*-acetyl-2-deoxy-L-sorbopyranos-2,3-ene[1]

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(Received November 18, 1967)

An acid-catalyzed reaction in acetic anhydride was found to isomerize 1,3,4,5-tetra-*O*-acetyl-2-deoxyl-L-sorbopyranos-2,3-ene (V) to four new unsaturated compounds. When the reaction was allowed to continue for a longer period, they underwent polymerization, but did not afford 2-hydroxyacetylfuran acetate (XXVIb). The reaction in acetic acid containing water was shown to mainly convert V into XXVIb. This reaction pathway was thought to be different from the above.

Dehydrochlorination of 1,3,4,5-tetra-*O*-acetyl-α-L-sorbopyranosyl chloride (IV),[2,8] derived from L-sorbose (I), through the agency of mercuric cyanide,[4,5] yields 1,3,4,5-tetra-*O*-acetyl-2-deoxy-L-sorbopyranos-2,3-ene (V). This communication is concerned with isomerizations of this unsaturated compound.

The isomerizations and other reactions of acylated aldo-1-enoses have recently received considerable attention.[6,7] The facile dissociation of the C_3-substituent in these compounds is readily understood as resulting from activation of the C_3-position toward carbonium ion formation by the allylic double bond.[8] The activation is especially strong for 1-enose structures since the ring oxygen can participate in charge

1) Sorboses. Part XI. For Part X, see T. Maeda, K. Tori, M. Ohtsuru and K. Tokuyama, This Bulletin, **41**, 191 (1968).
2) K. Tokuyama and M. Katsuhara, This Bulletin, **39**, 2728 (1966).
3) H. H. Schlubach and G. Graefe, *Ann.*, **532**, 211 (1937).
4) R. U. Lemieux and D. R. Linback, *Can. J. Chem.*, **43**, 94 (1965).
5) B. Coxon, *Tetrahedron*, **22**, 228 (1966).
6) B. Helferic, *Adv. Carbohydrate Chem.*, **7**, 209 (1952).
7) J. Staněk, M. Cerný, J. Kocourek and J. Pacâk, "The Monosaccharides," Academic Press Inc., New York (1963), p. 384.
8) H. S. Isbell, *J. Res. Natl. Bur. Stand.*, **A32**, 45 (1944).

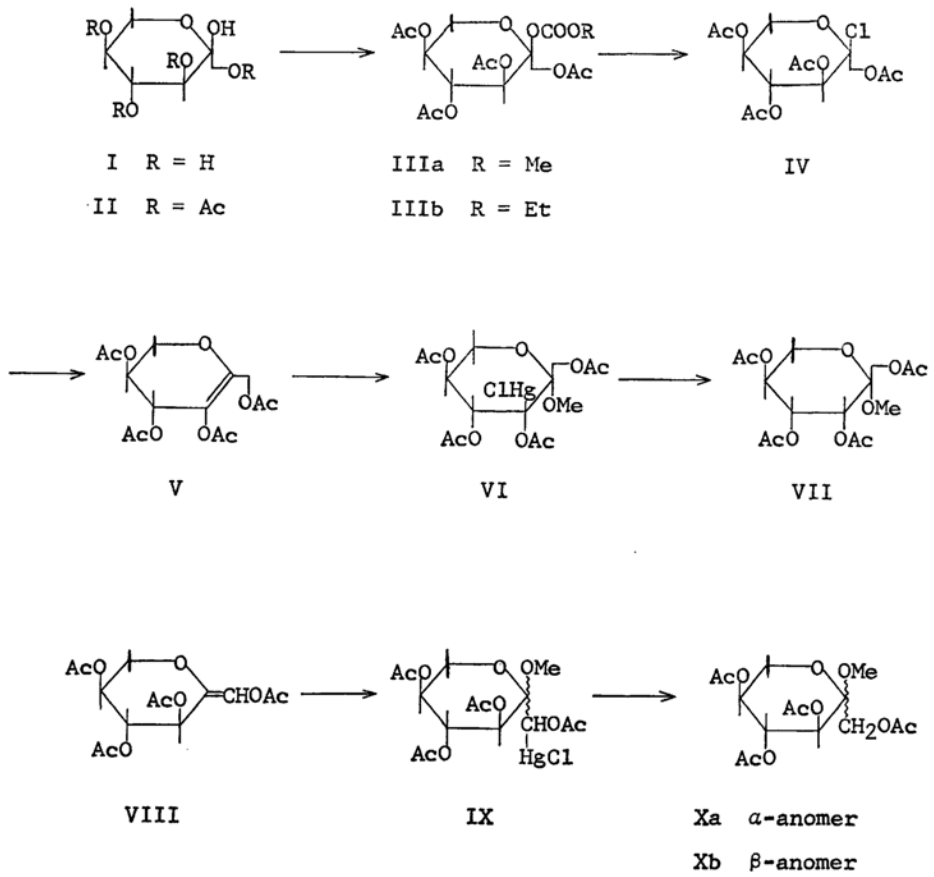


Chart 1.

delocalization.[9-13] It was anticipated that V would undergo similar isomerization, which pathway may provide interesting information regarding the acid-catalyzed degradation of ketohexose to 2-hydroxyacetylfuran (XXVIa)[14,15] through 2,3-enolization with the elimination of the hydroxyl group at the allylic C_4-position.[16,17]

The structure of V was confirmed by methoxymercuration[18] and NMR spectroscopy. NMR data obtained by 1st-order approximation are reported in Tables 1 and 2. The methoxymercuration of V gave a mercurichloride (VI). Reductive demercuration of VI with sodium borohydride in the presence of pyridine was accompanied by deacetylation, and yielded a methyl glycoside, which was isolated as a tetraacetate (VII).[19] Despite its large positive value of optical rotation, VII was not identical with methyl 1,3,4,5-tetra-*O*-acetyl-β-L-sorbopyranoside (Xb).[8] Thus, VII was concluded to be methyl 1,3,4,5-tetra-*O*-acetyl-β-L-tagatopyranoside.[20,21] The formation of the tagatopyranoside (VII) supports the structure of V, because another possible isomer VIII from the dehydrochlorination of IV should yield X *via* IX.

The NMR spectrum of V in chloroform-d (Fig. 1a) showed four singlets at about τ 7.9 due to acetoxyls, a somewhat broad singlet at τ5.39 due to H_1 (see also Fig. 1h) and signals due to H_6, $H_{6'}$, H_5, and H_4 as an ABXY pattern. This assignment

9) R. J. Ferrier and G. H. Sankey, *J. Chem. Soc.* (*C*), **1966**, 2339, 2345.
10) R. J. Ferrier, *ibid.*, **1964**, 5443.
11) D. M. Cement and R. J. Ferrier, *ibid.*, **1966**, 2830.
12) R. U. Lemieux, D. R. Linback, M. L. Wolfrom, F. B. Moody, E. G. Wallace and F. Komitsky, Jr., *J. Org. Chem.*, **30**, 1092 (1965).
13) R. K. Ness and H. G. Fletcher, Jr., *ibid.*, **28**, 435 (1963).
14) C. J. Moye, *Australian J. Chem.*, **19**, 2317 (1966)
15) R. E. Miller and S. M. Cantor, *J. Am. Chem. Soc.*, **74**, 5236 (1956).
16) E. F. L. J. Anet, *Chem. & Ind.*, **1962**, 262.
17) E. F. L. J. Anet, *Adv. Carbohydrate Chem.*, **19**, 181 (1964).
18) K. Tokuyama, E. Tsujino and M. Kiyokawa, This Bulletin, **38**, 1344 (1965).
19) G. R. Inglis, J. C. P. S. Schwartz and L. McLaren, *J. Chem. Soc.*, **1962**, 1014.
20) The evidence of NMR indicates that the favorable conformation of VII in chloroform-d is the Cl chair form. See Ref. 21.
21) C. V. Holland, D. Horton and J. S. Jewell, *J. Org. Chem.*, **32**, 1818 (1967).

TABLE 1. CHEMICAL SHIFTS (τ)[a]

Compound	H_6	$H_{6'}$	H_5	H_4	H_3	H_1 and $H_{1'}$	CH_3COO	Other signal
IIIa	6.00	6.29	4.88	4.46	4.73	5.32, 5.43	7.93, 7.96(2) 8.00	$COOCH_3$ 6.19
IIIb	5.93	6.38	4.90	4.46	4.74	5.32, 5.45	7.93, 7.96(2) 8.00	$COOCH_2CH_3$ 5.70 $COOCH_2CH_3$ 8.66
IV	5.88	6.08	4.92	4.44	4.72	5.57, 5.77		
V	5.72	5.97	5.04	4.61	—	5.39	7.89, 7.91 7.95(2)	
VI	5.92	6.22	5.08	4.41	—	5.46, 6.16	7.77, 7.80 7.92(2)	OCH_3 6.59
VII	5.89	6.23	5.09	4.70	4.59	5.76, 5.82	7.87, 7.92 7.91, 7.94	OCH_3 6.65
XII[b]	6.00	6.24	4.85	4.17	—	2.67[c]	8.27, 8.31 8.33	
XIV	5.67	5.95	5.04	4.55	—	2.55[c]	7.86, 7.90(2) 7.91, 7.94	
XV	5.23	5.38	2.88	3.70	—	2.92[c]	7.88, 7.93 7.95	
XX[b]	~5.51 ~6.14		2.94 3.92	3.89 4.12	— —	5.56 5.39	7.94 8.32	OCH_3 6.58 OCH_3 6.94
XXI	6.07	6.56	4.78	5.50	4.52	5.90	7.86, 7.91 7.95	OCH_3 6.71
XXII	5.80	6.23	4.83	5.58	4.65	5.79	7.85(2) 7.88	OCH_3 6.63
XXIV	5.61	5.94	4.96	4.79	4.06	0.74[c,d]	7.91, 7.94	

a) In chloroform-d (unless otherwise stated). b) In benzene-d_6. c) One proton.
d) Aldehyde proton.

TABLE 2. COUPLING CONSTANTS (cps)[a]

Compound	$J_{6,6'}$	$J_{5,6}$	$J_{5,6'}$	$J_{4,6}$	$J_{4,6'}$	$J_{4,5}$	$J_{3,5}$	$J_{3,4}$	$J_{1,4}$	$J_{1,1'}$
IIIa	11.2	5.8	11.2	—	—	9.7	1.5	8.4	—	11.8
IIIb[c]	10.4	5.7	10.4	—	—	10.1	1.0	8.3	—	11.5
IV	10.6	5.3	10.6	—	—	9.0	1.0	9.0	—	12.3
V	12.3	2.4	1.5	1.3	—	2.7	—	—	0.5	0
VI	13.2	2.4	1.3	—	1.3	3.7	—	—	—	12.0
VII	13.1	2.1	1.3	—	1.3	3.8	—	3.8	—	11.8
XII[b]	12.1	2.2	2.8	0.7	—	6.2	—	—	0.7	—
XIV	12.5	2.7	1.8	1.5	—	2.7	—	—	—	—
XV	18.4	2.4	3.6	2.4	1.8	11.0	—	—	—	—
XX	d)	2.4	3.4	2.0	2.0	10.5	—	—	—	d)
XXI	10.3	5.7	10.3	—	—	10.8	—	3.1	—	d)
XXII	13.2	3.0	1.6	—	1.6	3.0	—	4.4	—	d)
XXIV	12.4	3.0	2.0	1.7	—	3.0	1.4	5.0	—	—

a) In chloroform-d unless otherwise stated. b) In benzene-d_6. c) $COOCH_2CH_3$: $J_{CH_2,\ CH_3}$=7.0.
d) Obscured.

was confirmed by decoupling experiments (Fig. 1b—1g). Double irradiation at the center of resonance frequencies of H_6 and $H_{6'}$ (Fig. 1b) changed the 8-line multiplet of H_5 into a doublet ($J_{4,5}$ 2.7 cps) and the 8-line multiplet of H_4 into a somewhat broad doublet. By double irradiation on $H_{6'}$, the H_5 signal collapsed to a doublet-doublet ($J_{5,6}$ 2.4 cps), but no changes in the H_4 signal were observed (Fig. 1c). By double irradiation on H_6, the H_5 signal collapsed to a doublet-doublet and the H_4 signal to a somewhat broad doublet (Fig. 1d). Conversely, decouplings of H_4 (Fig. 1f) and H_5 (Fig. 1g) resulted in changes of the signals of H_5 and H_6 ($J_{5,6'}$ 1.5 cps) and of those of H_4, H_6 and $H_{6'}$ ($J_{6,6'}$ 12.3 cps and $J_{4,6}$ 1.3 cps), respectively. Decoupling of H_1 (Fig. 1e) made the broad signal

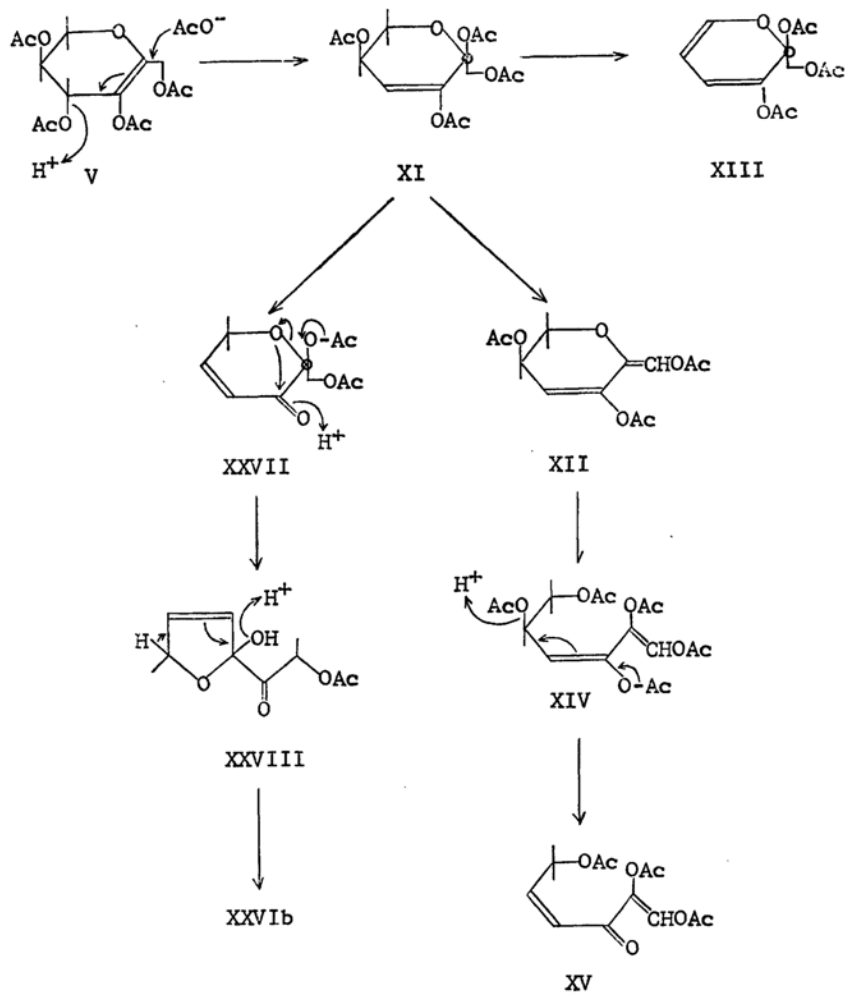


Chart 2.

of H_4 relatively sharper, showing the presence of homoallylic coupling between C_4 and C_1 protons. These observations provided evidence for the structure of V. Applying the Karplus correlation[22] for the coupling constants obtained and the "W-letter" rule[23] for the long-range spin coupling between H_4 and H_6, we reached the conclusion that V should exist in H_1 conformation.[24]

It was found that the treatment of V in acetic anhydride containing *p*-toluenesulfonic acid (TsOH) resulted in rapid formation of a mixture of at least four products (A, B, C, and D) in the thin-layer chromatograms. When the reaction was interrupted at the initial stages, the product A was mainly isolated. On the other hand, when the reaction was allowed to proceed for 48 hr, products B and C were detected as major products. These products could be resolved by preparative thin-layer chromatography using several solvent systems. The structures established for the new compounds described above were confirmed by the application of NMR spectroscopy with the use of spin decoupling to assign the origins of the signals. The assignment was also based on the chemical shifts with reference to those of V.

As it is expected that the reaction of V under acidic conditions undergoes allylic displacement of the C_4-ester grouping and the formation of a 3,4-unsaturated compound (XI),[8-13] the structure of compound A was thought to be XI or its derivative. The analytical data and the integration of an NMR spectrum determined it as a triacetate $C_{12}H_{14}O_7$, which was thought to be derived from XI by the elimination of one mole of acetic acid. The elimination may occur at the 1,2- or 5,6-position. Thus, the

22) M. Karplus, *J. Chem. Phys.*, **30**, 11(1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).
23) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco (1964), p. 115.
24) R. J. Ferrier and W. G. Overend, *Quart. Rev.*, **13**, 265 (1959).

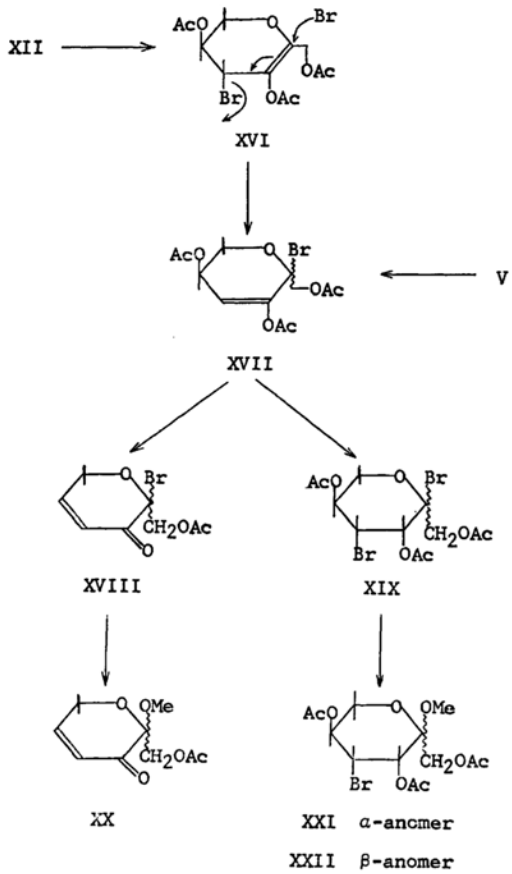
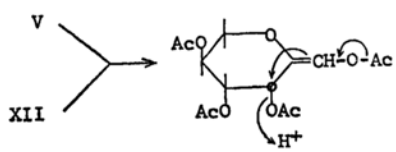
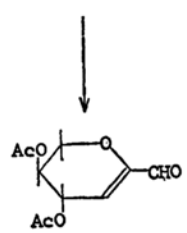


Chart 3.





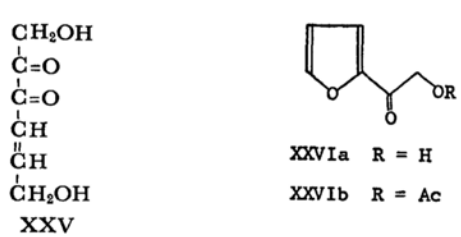
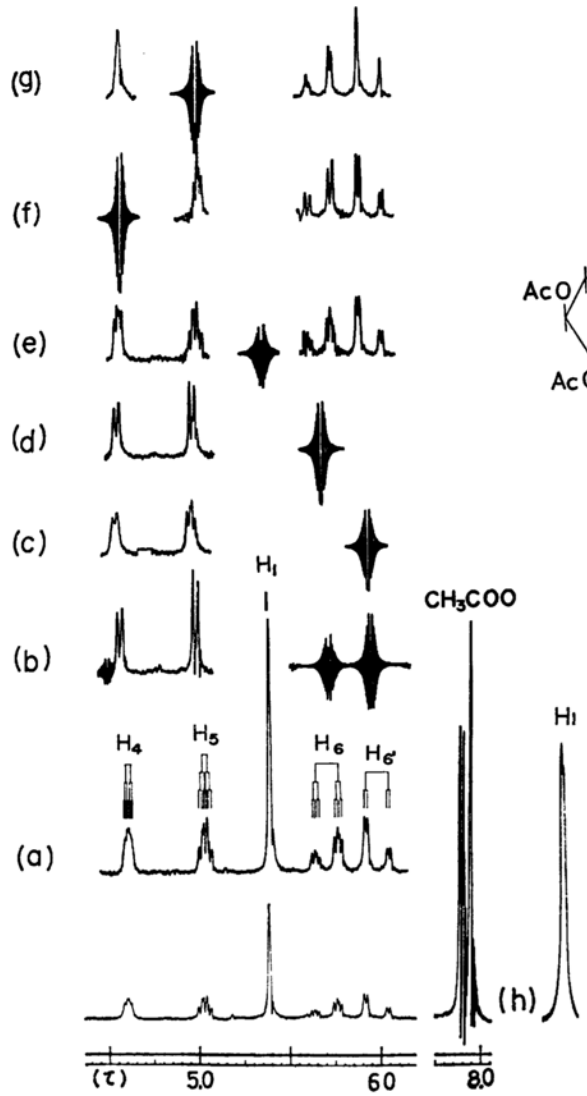


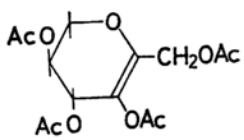
Chart 4.

structure is proposed to be XII or XIII. The UV and IR spectra showed the characteristic bands due to a conjugated diene and the NMR spectrum (Fig. 2) revealed the presence of C_6-methylene protons and an olefinic C_1-proton. The results clearly support the structure of XII. Figure 2a shows the assignment of the NMR spectrum in benzene-d_6. The rough, 1-proton singlet at τ2.67 should arise from the olefinic H_1. Its lower chemical shift is understandable in view of acetoxy substituent on the ethylenic group. The signals of the other protons (H_6, $H_{6'}$, H_5 and H_4) appear as the pattern of ABXY system, an AB quartet at τ6.00 (H_6) and 6.24 ($H_{6'}$), an 8-line multiplet (X part) at τ4.85 (H_5) and a 6-line multiplet (Y part) at τ4.17 (H_4). On double irradiation at the C_6-methylene position, the H_5 multiplet collapsed to a sharp doublet ($J_{4,5}$ 6.2 cps) and the H_4 multiplet to a doublet-doublet (Fig. 2b), showing the presence of long-range coupling between H_1 and H_4 ($J_{1,4}$ 0.7 cps). Double irradiation at the H_6 position caused the H_4 multiplet to collapse to a doublet-doublet (Fig. 2c), but double irradiation at the $H_{6'}$ position did not cause any changes of the H_4 signal (Fig. 2d). These decoupling experiments confirmed the above-described assignment (Fig. 2a), which is consistent with structure **XII.**

The reaction of XII with hydrogen bromide in benzene followed by glycosidation with methanol gave three pyranosides XX, XXI and XXII as major products. XX gave analytical data corresponding to methyl glycoside monoacetate, $C_9H_{12}O_5$, and its IR and UV spectra revealed bands due to an α,β-unsaturated ketone. The NMR spectrum in chloroform-d (Fig. 3) showed two singlets at τ7.94 due to one acetyl methyl and at τ6.58 due to one methoxy methyl, 2-proton singlet at τ5.56 due to C_1-protons and an AB type quartet of ABXY system due to C_6-protons at about τ5.5. The above-described data established the structure XX. The remaining two 1-proton multiplets at τ2.94 and 3.89 due to olefinic protons were assignable to H_5 and H_4, which are coupled to each other (J 10.5 cps), and the latter showed allylic coupling with C_6-methylene protons. These observations provided further proof for the structure XX. Evidence bearing on the anomeric configuration of XX was not obtained.

Analytical data and optical rotation showed that XXI was a methyl bromo-tri-*O*-acetyl-α-L-glycoside, $C_{13}H_{19}O_8Br$. The NMR spectrum showed a 2-proton singlet at τ5.90 due to C_1-protons, an AB type quartet of ABX system at τ6.07 (H_6) and 6.56 ($H_{6'}$) due to C_6-protons, an 8-line multiplet at τ4.78 due to H_5, a doublet-doublet at τ5.50 due to H_4 and a doublet at τ4.52 due to H_3. The relatively lower chemical shifts of H_3 and H_5 than H_4 determined the position of the bromine to be at the C_4-position. The coupling constants ($J_{3,4}$ 3.1 cps and $J_{4,5}$ 10.8 cps) suggest that the relationship of H_3 and H_4 should be *cis* (equatorial-axial) and that of H_4 and H_5 be trans





V

Fig. 1. NMR spectra of V in chloroform-d at 100 Mc.

(axial-axial).[25] Therefore, the structure of XXI was clearly determined as methyl 1,3,5-tri-*O*-acetyl-4-bromo-4-deoxy-α-L-tagatopyranoside.[26,27]

Treatment of XXII with hydrogen chloride in benzene followed by glycosidation with methanol gave XXI. Thus, it was determined to be the β-anomer of XXI.

The reaction process of the formation of these pyranosides is considered as shown in Chart 3. The 1,4-addition of hydrogen bromide to XII afforded XVI, which was then converted into XVII by an allylic displacement reaction with hydrogen bromide. Two reaction pathways can exist for the further reaction of XVII. The first is the addition of hydrogen bromide to the 3,4-double bond yielding XIX which is transformed to glycosides XXI and XXII. The preferable formation of tagatopyranosides is thought to be caused by the anchimeric effect of the acetoxy group at the C_5-position.[28,29] The second is the formation of XVIII, which may be formulated

25) R. H. Bible, "Interpretation of NMR Spectra," Plenum Press, New York (1965), p. 35.

26) The evidence of NMR indicates that the favored conformation of XXI is the 1C chair form. See, Ref. 27.

27) F. W. Lichtenthaler and H. K. Yahya, *Tetrahedron Letters*, **1965**, 1805.

28) Formation of 4,5-acetonium ion[29] may be thought on the protonation of XVII. In this ion form, the C_3-acetoxy group might be expected to predominantly be trans to 4,5-acetonium group.

29) H. Paulsen, W. P. Trautwein, F. G. Espinosa and K. Heynes, *Tetrahedron Letters*, **1966**, 4131.

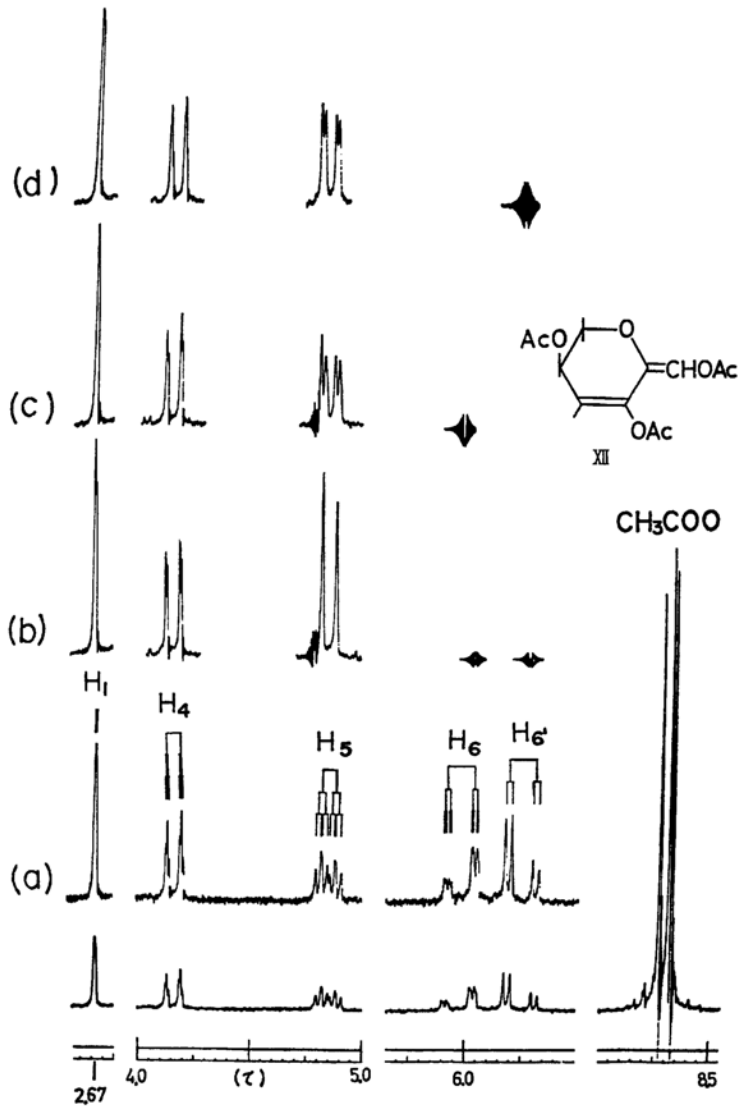


Fig. 2. NMR spectra of XII in benzene-d_6 at 100Mc.

as an elimination of the acetoxy group of the C_5-position to form an allylic cation, followed by loss of a C_8-acetyl cation. XVIII is converted into XX by methanolysis.

The same results were obtained in the treatment of V under the same reaction conditions, in which the formation of XVII is very probable. Therefore, the above pathway and, consequently, the structure XII were confirmed.

The compound B had the correct analysis for XII plus one mole of acetic anhydride and had a conjugate diene absorption in the infrared. It was also derived from the acid treatment of XII in acetic anhydride. Therefore, its structure should be XIV, which is the ring-open form of XII. The fact that the NMR data in chloroform-d are quite similar to those of XII supported this structure. The spectrum (Fig. 4a) contained singlets at about τ7.9 due to five acetoxyls, a noisy singlet at τ2.55 due to olefinic H_1, an AB type quartet of ABXY system at τ5.67 (H_6) and 5.95 ($H_{6'}$) due to C_6-protons, a 6-line multiplet at τ5.04 due to H_5 (X part) and a doublet-doublet at τ4.55 due to H_4 (Y part). Double irradiation at the H_4 position (Fig. 4b) caused the collapse of the H_5 and H_6 signals to doublet-doublets ($J_{5,6'}$ 1.8 and $J_{5,6}$ 2.7 cps), while double irradiation at the H_5 position caused the collapse of the H_4, H_6 and $H_{6'}$ signals to a somewhat broad doublet, a doublet-doublet ($J_{4,6}$ 1.5 cps) and a doublet ($J_{6,6'}$ 12.5 cps), respectively (Fig. 4c). The somewhat broad signals of H_4 and H_1 imply the presence of weak long-range spin coupling between them. Thus, the structure XIV was established.

The combined data of chemical analysis, the UV

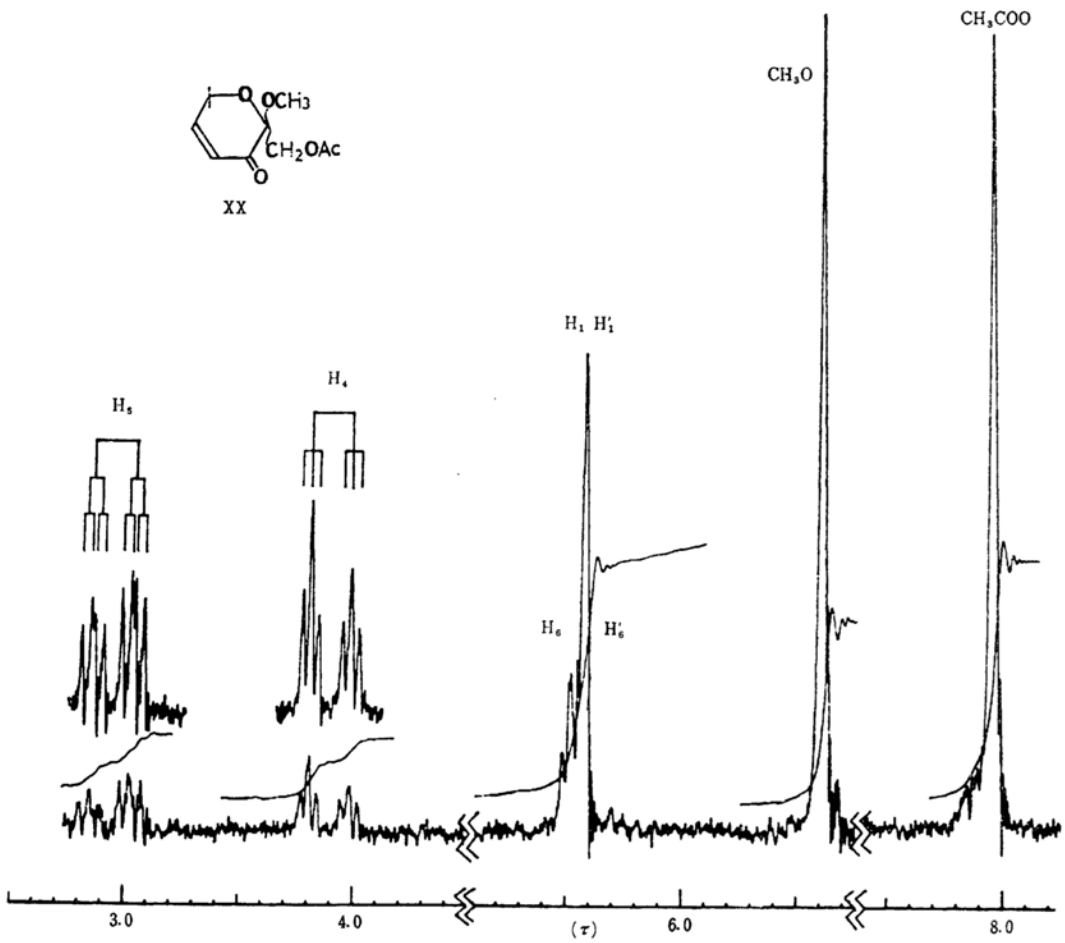


Fig. 3. NMR spectrum of XX in chloroform-d at 60Mc.

and IR spectra established that compound C was a conjugate ketone compound with an elementary composition corresponding to that of XIV minus one mole of acetic anhydride. It was also derived from the acid-treatment of XIV. As elimination of the acetoxy group at allylic C_5-position and an acetyl group at the C_6-position of XIV are reasonably expected,[30,31] its structure was concluded to be XV. In chloroform-d, XV displayed a well-resolved spectrum (Fig. 5) with three acetoxyl singlets at about τ7.9, a singlet at τ2.92 due to H_1 and an ABXY pattern of a 8-line multiplet at τ3.70 (Y part), an 8-line multiplet at τ2.88 (X part) and an AB quartet at τ5.23 and 5.38 due respective to olefinic H_4 and H_5, which are coupled to each other, and to methylene H_6 and $H_{6'}$. The double irradiation at the center of resonance of H_5 (Fig. 5b) changed the signals of H_4, H_6 and $H_{6'}$ into doublet-doublet. On double irradiation on C_6 protons (Fig. 5c), the signals of H_4 and H_5 collapsed into doublets ($J_{4,5}$ 11.0 cps), showing the presence of allylic coupling between C_4 and C_6 protons. These irradiation experiments supported the structure XV.

The formation of the compound D was also observed at the initial stage of the reaction of V as a minor product. The analytical data corresponded to a diacetate, $C_{10}H_{12}O_6$, showing IR bands due to an α,β-unsaturated aldehyde. Thus, this was tentatively assigned to XXIV. The NMR spectrum (Fig. 6a) showed unequivocally the presence of an aldehyde at τ0.74. An AB quartet due to C_6-methylene at τ5.61 and 5.94, multiplet at τ4.96 due to H_5 and at τ4.79 due to H_4 and a doublet-doublet at τ4.06 due to H_3 are also easily analyzed as an ABXY pattern. The chemical shifts show that H_3 should be an olefinic proton and acetoxy groups should be at the C_4- and C_5-positions. Therefore, the structure of compound D was determined to be XXIV. Double irradiation at H_3 (Fig. 6b), giving a pattern similar to that of V (Fig. 1), also supported the structure.

30) E. F. L. J. Anet, *Chem. & Ind.*, **1963**, 1035.
31) E. F. L. J. Anet, see Ref. 14, p. 195.

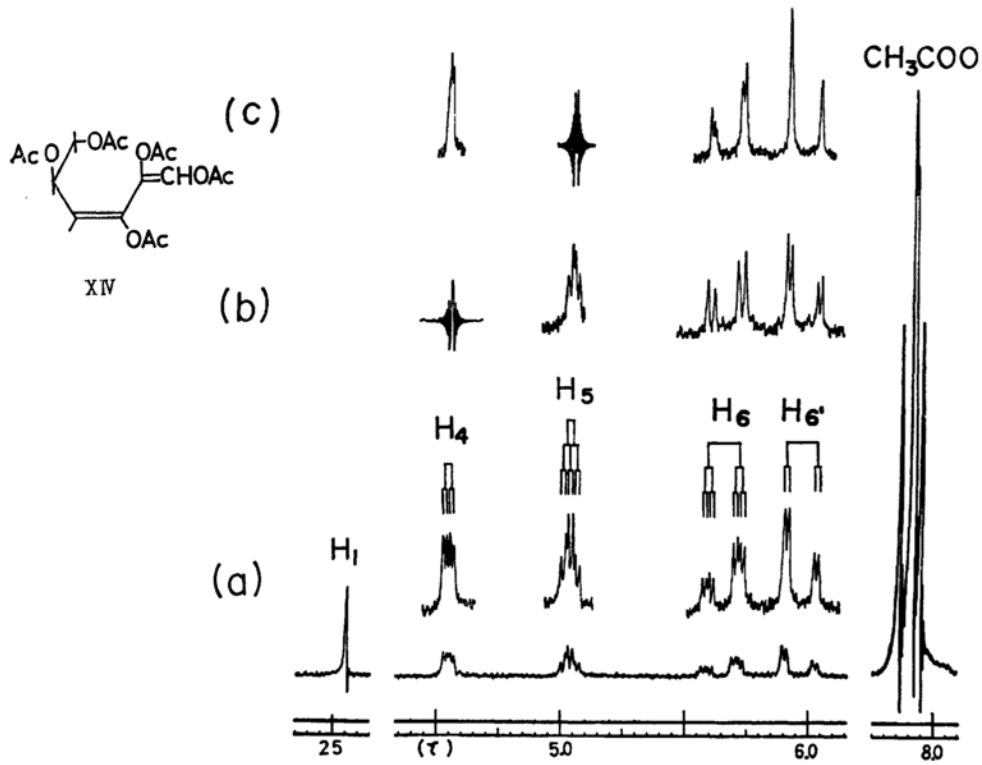


Fig. 4. NMR spectra of XIV in chloroform-d at 100Mc.

Thin-layer chromatographic studies on the above-described degradation of V in acetic anhydride showed that the initial products were primarily XII and a minor amount of XXIV. When the reaction was allowed to continue for longer periods of time, the amounts of XIV and XV increased at the expense of XII. Under similar acidic conditions, the conversion of XIV into XV was also observed, however, the reverse reactions XV→XIV and XIV→XII were not observed. Consequently, the reaction process of the degradation of V is concluded to proceed *via* a pathway of V→(XI)→XII→XIV→XV as shown in Chart 2.[32] No isolation of XI must be caused by its instability.[33]

It is quite natural to consider that the precursor of XXIV should be a 1,2-ene derivative, VIII or its epimer XXIII. The elimination of a protonated C_3 acetoxy group of VIII or XXIII, followed by the loss of C_1 acetyl cation yielded XXIV. For the formation of VIII or XXIII, two possible pathways can be proposed. One is the 3,4 addition of acetic acid to XII and the other is the rearrangement of the 2,3-double bond of V into 1,2-position; however, the latter is favorable, since thin-layer chromatographic data elucidated no formation of XXIV by acid-treatment of XII in acetic anhydride or in acetic acid.

Anet's mechanism for the acid-catalyzed degradation of hexose to furans proposed that a key intermediate is an unsaturated osone such as XXV which may be converted into XXVIa. As the deacetylated form of XV is quite similar to XXV, it is expected that XV may also be converted into XXVI. However, the possibility of the above-described intermediates XII, XIV and XV being the precursor of furans is excluded, since heating them in an acetic anhydride medium only gave polymeric substances.

The treatment of V in acetic anhydride also did not afford furans even under stronger conditions, however, treatment in acetic acid yielded XXVIb. Since the UV absorption spectrum of XXVIb gave an absorption maximum at 272 mμ, it was felt that furan formation could be followed by observing the appearance of this peak. Solutions were made of V (1%) in acetic acid containing different concentrations of water and the absorbance of each solution at 272 mμ was recorded after heating at 95°C for 4.5 hr. The results, as shown in Fig. 7, revealed that the formation of XXVIb tended to increase with increasing addition of water. Although XII was detected at the initial stages of these reactions, it yielded

32) This pathway *via* XI was thought to be more favorable than a pathway of V→XII→XIV→XV, since the formation of XX (XVII) was observed in the reaction of V with hydrogen bromide.

33) It was supposed that the two large substituents, of the C_2 position, OAc and CH_2OAc, make the molecule unstable.

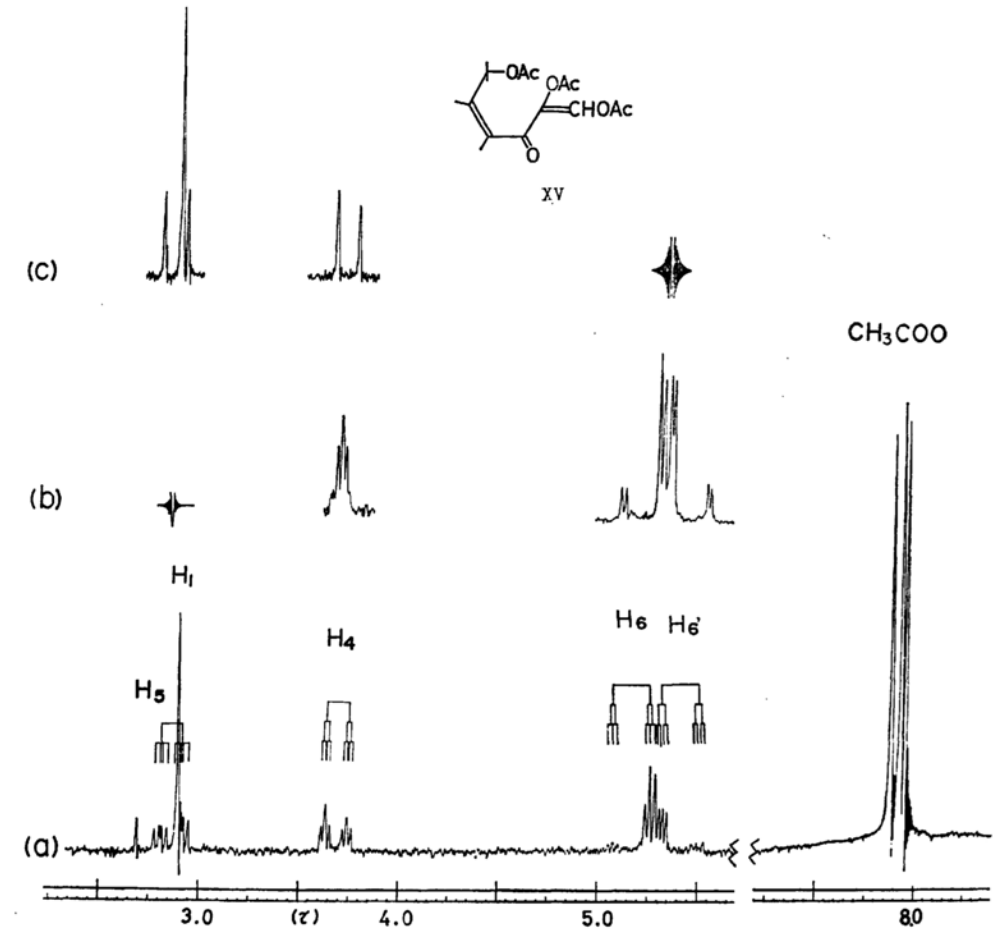


Fig. 5. NMR spectra of XV in chloroform-d at 100 Mc.

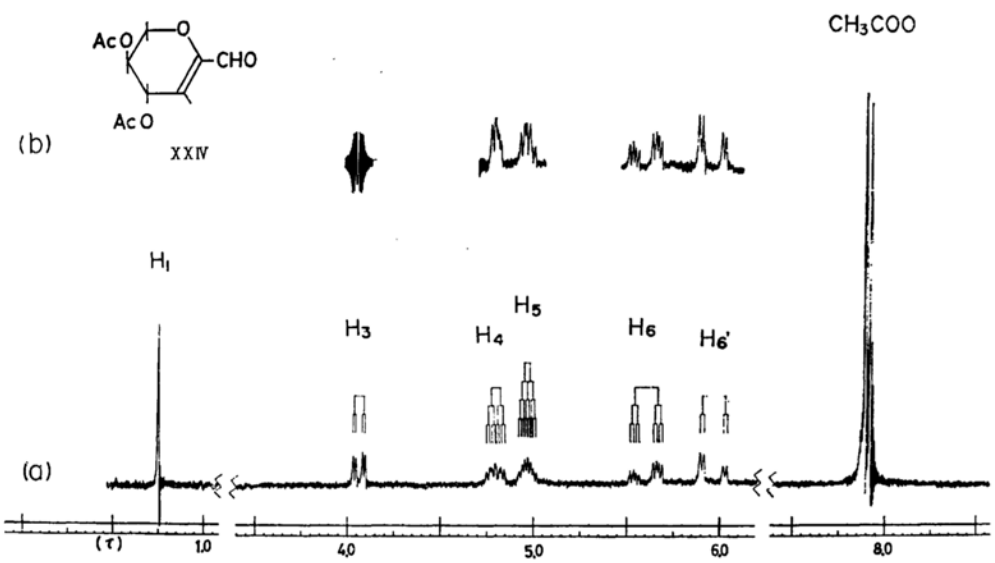


Fig. 6. NMR spectra of XXIV in chloroform-d at 100 Mc.

only traces of XXVIb under the same reaction conditions. Intermediates XIV and XV were hardly detected in the reaction mixtures and did not afford XXVIb in acetic acid-water. On the other hand, heating of another type of osone, XX, easily gave XXVIb. Therefore, the reaction process of the degradation of V to XXVIb is assumed to be as follows: V→XI→XXVII→XXVIII→XXVIb (see Chart 2). Attempts were made to isolate unknown osone XXVII from an acetic acid solution of V, but a complex mixture of products were isolated. By preparative thin-layer chromatography of the mixture, a compound showing IR and UV bands due to conjugate ketone and a quite similar pattern of NMR spectrum to XX was isolated, and was easily converted into XXVIb. Therefore, this thought to be XXVII, however, an adequate amount for determination of its correct structure was not obtained.[34-36]

It was somewhat surprising that the presence of water is very important for the degradation of V; it degradates to form polymeric substances under anhydrous conditions and to form furan XXVIb by aqueous treatment.

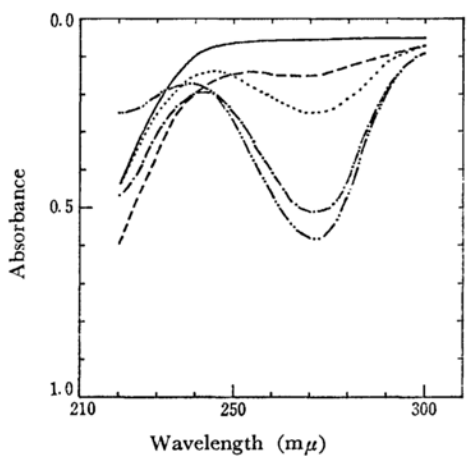


Fig. 7. The formation of XXVIb from V (at 95°C for 4.5hr).

a) acetic acid only (without V) ——
b) in acetic acid — — —
c) in acetic acid containing 10% of water - - - -
d) in acetic acid containing 50% of water —·—·
e) in acetic acid containing 90% of water —··—

Experimental

Melting points were determined on a Kofler block. The NMR spectra were measured on a Varian A-60 spectrometer at 60 Mc at room temperature using tetramethylsilane (TMS) as internal reference. Spectra at 100 Mc were obtained at room temperature from Varian HA-100 instrument internally locked on TMS in the frequency-sweep mode of operation. NMR data obtained by 1st-order approximation were summarized in Tables 1 and 2.

Thin-layer chromatography was performed on a silica gel plate. The solvent-systems used were ether-petroleum ether (3: 1, v/v, solvent A, 2: 1, v/v, solvent B and 1: 2, v/v, solvent C), benzene-ether (3: 1, v/v, solvent D), chloroform-acetone (60: 1, v/v, solvent E) and ethyl acetate-petroleum ether (2: 3, v/v, solvent F). The separated materials were developed with either iodine vapor or 0.2% resorcinol in 10% ethanolic phosphoric acid, and then heated in an oven.[37] In the cases of preparative thin-layer chromatography, the developed zones were extracted with acetone unless otherwise stated. The evaporation of the acetone under reduced pressure gave the materials.

The optical rotations were determined in a 10cm microtube in chloroform containing 1% of ethanol, and concentrations were recorded in percentage. The UV spectra were measured in ethanol.

1,3,4,5-Tetra-*O*-acetyl-2-*O*-carbomethoxy-α-L-sorbopyranose (IIIa). A mixture of II (10 g),[38] dimethyl pyrocarbonate (8 m*l*)[39,40] and potassium carbonate (0.1 g) was warmed at 50—60°C for 1.5 hr with stirring. The reaction mixture was filtered and washed with ether. The washings and the filtrate were combined and then evaporated under reduced pressure. The residue was recrystallized from ether to give colorless columns (6.9 g), mp 117—117.5°C, $[\alpha]_D^{22}$ −63.2° (*c* 1.038).

Found: C, 47.59; H, 5.58%. Calcd for $C_{16}H_{22}O_{12}$: C, 47.29; H, 5.46%.

1,3,4,5-Tetra-*O*-acetyl-2-*O*-carboethoxy-α-L-sorbopyranose (IIIb). A mixture of II (30 g), diethyl pyrocarbonate (23 m*l*) and potassium carbonate (0.3 g) was warmed at 50—55°C for 0.5 hr with stirring. IIIb (38.9 g) was obtained in a manner similar to IIIa. IIIb had mp 96—97°C, $[\alpha]_D^{22}$ −69.7° (*c* 1.116).

Found: C, 48.73; H, 5.92%. Calcd for $C_{17}H_{24}O_{12}$: C, 48.57; H, 5.76%.

1,3,4,5-Tetra-*O*-acetyl-α-L-sorbopyranosyl Chloride (IV). A solution of IIIb (30 g) in acetic acid (600 m*l*) saturated with anhydrous hydrogen chloride was kept at 0—5°C for 3.5 hr. The solution was added to chloroform (500 m*l*) and washed with ice-water, saturated aqueous sodium bicarbonate and ice-water,

34) Another new compound was isolated, which gave analytical data corresponding to $C_{12}H_{14}O_7$. Its NMR spectrum in chloroform-d at 60 Mc revealed three 3-proton singlets at τ 7.73, 7.92 and 7.94 due to acetoxyls, one 1-proton singlet at τ 3.51 and two 2-proton singlets at τ 4.99 and 5.01. Therefore, the structure was tentatively assigned to be 2,5-diacetoxymethyl-3-acetoxyfuran. Although further evidence seems to be required, a related experiment that D-glucal smoothly yielded 2-methoxymethyl-5-hydroxymethylfuran with methanolic hydrochloric acid seems support this structure (see Refs. 35 and 36).

35) F. Shafizadeh and M. Stacey, *J. Chem. Soc.*, **1952**, 3608.

36) D. Horton and T. Tsuchiya, *Carbohydrate Res.*, **2**, 349 (1966); *ibid.*, **3**, 257 (1966).

37) A. Anno and N. Seno, "Jikken Kagaku Kōza," Bd. 23, ed. by Chem. Soc. Japan, Maruzen, Tokyo (1957), p. 374.

38) Y. Khounine and G. Arragon, *Bull. Soc. Chim. France*, **1938**, 1404.

39) Kindly supplied by Dr. Shinzaburo Sumimoto of this Laboratory. S. Sumimoto, Japanese Pat. 42-19818 (1967).

40) M. Fujimoto, Japanese Pat. 42-12272 (1967).

and dired. Removal of the solvent gave a crude chloride (24.5 g) which was purified by silica gel chromatography with benzene. From 1.55 g of the crude syrup, using 30 g of silica gel, a colorless syrup (0.36 g) was obtained. The recrystallization of the syrup from ether and petroleum ether gave pure IV (0.15 g), mp 67.5—69.5°C, which was identical with an authentic sample.[2,8] IV was also prepared from IIIa in a similar way.

1,3,4,5-Tetra-*O*-acetyl-2-deoxy-L-sorbopyranos-2,3-ene (V). To a suspension of mercuric cyanide (19.9 g) in dry benzene (400 m*l*), a dry benzene solution (100 m*l*) of crude IV (24.5 g) was added. Traces of water were removed by azeotropic distillation with benzene (*ca.* 20 m*l*). After it had been refluxed for 8 hr with stirring, the reaction mixture was filtered and the filtrate was evaporated. The residue was extracted with chloroform (500 m*l*) and the chloroform was washed with 30% potassium iodide solution and then water and dried. Removal of the chloroform gave a dark brown syrup (18 g). The purification of the syrup on alumina column chromatography (135 g of alumina was used) with benzene gave V as a colorless syrup (13.7 g), $[\alpha]_D^{22}$ +217.6° (*c.* 1.032).

Found: C, 50.95; H, 5.51%. Calcd for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49%. UV_{max} 209 mμ (ε 8800).

Methyl 1,3,4,5-Tetra-*O*-acetyl-3-*C*-chloromercuri-β-L-tagatopyranoside (VI). To a solution of mercuric acetate (1.05 g) in absolute methanol (20 m*l*), V (1.0 g) was added. After the mixture had stood overnight at room temperature, the solvent was removed and extracted with chloroform. The chloroform solution was shaken with saturated aqueous sodium chloride (100 m*l* ×2), washed with saturated aqueous sodium bicarbonate and water, dried and the solvent removed. The syrup (1.07 g) which was obtained was purified by preparative thin-layer chromatography (solvent A, R_f, 0.20). The purified syrup (0.21 g) was recrystallized from ethanol to give colorless columns (0.12 g), mp 184—189°C, $[\alpha]_D^{23}$ +71.1° (*c* 1.017).

Found: C, 30.72; H, 3.62; Hg, 32.96%; mol wt, 588. Calcd for $C_{15}H_{21}O_{10}HgCl$: C, 30.16; H, 3.54; Hg, 33.58%; mol wt, 597.385.

Methyl 1,3,4,5-Tetra-*O*-acetyl-β-L-tagatopyranoside (VII). Sodium borohydride (50 mg) was added as a solid in five portions, at intervals, to a pyridine solution (5 m*l*) of VI (0.7 g). After being kept at room temperature for 2.5 hr, the reaction mixture was filtered and washed with pyridine (5 m*l*). Acetic anhydride (10 m*l*) was added to a combined solution of the filtrate and the washings. The solution was allowed to stand overnight at room temperature, and then poured onto ice, made alkaline with sodium carbonate, and extracted with chloroform. The extract was washed with 5% sulfuric acid, water and dried, after which the solvent was removed under reduced pressure. The purification of the residue by preparative thin-layer chromatography (solvent A, R_f 0.38, extracted with chloroform) gave crude crystals (205 mg). Recrystallization of the crystals from ether and petroleum ether gave colorless columns (83 mg), mp 87—87.5°C, $[\alpha]_D^{22}$ +104.2° (*c* 0.947).

Found: C, 49.67; H, 6.12%. Calcd for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12%.

Acid-catalyzed Isomerization of V in Acetic Anhydride.[41] A solution of V (6.68 g) in acetic anhydride (67 m*l*) containing 1% of TsOH was kept at 30°C for 24—48 hr (for 24 hr to obtain XII as a major product and for 48 hr to obtain XIV and XV as major products). The solution was then poured into ice-water (800 m*l*) under vigorous stirring, made alkaline with sodium bicarbonate and extracted with chloroform. The extract was washed with 5% aqueous sodium bicarbonate and water. The syrup (5.8 g) obtained on solvent removal from the dried extract was fractionated by preparative thin-layer chromatography. (i) From the syrup (3.6 g) obtained from the reaction for 24 hr, XII (0.40 g) was isolated as a syrup in a pure state by repeated preparative thin-layer chromatography (solvent D, R_f 0.65, extracted with ether). (ii) From the syrup obtained from the reaction for 48 hr, XIV, XV and XXIV were fractionated by thin-layer chromatography (solvent F, R_f 0.29 (XIV), 0.22 (XV), 0.4—0.7 (XXIV)). From the syrup (14.29 g), these were obtained in a crude state in the ratio of XIV (0.36 g), XV (0.46 g), and XXIV (0.94 g). XIV was recrystallized from ether (yield, 51 mg), and XV from ethanol (yield, 71 mg). XXIV was purified by repeated thin-layer chromatography (solvent E, R_f 0.61) (yield, 65.5 mg).

XII: Syrup $[\alpha]_D^{24}$ −88.0° (*c* 0.980). Found: C, 53.72; H, 5.73%; mol wt, 281. Calcd for $C_{12}H_{14}O_7$: C, 53.33; H, 5.22%; mol wt, 270.23. UV_{max} 261 mμ (ε 16100). $IR_{fil\,m}$ 1635 cm^{-1} (conj. C=C).

XIV: Colorless columns, mp 110—111.5°C, $[\alpha]_D^{22}$ +198.8° (*c* 0.997). Found: C, 49,44; H, 5.23%; mol wt, 387. Calcd for $C_{16}H_{20}O_{10}\cdot H_2O$: C, 49.23; H, 5.68%; mol wt, 390.34. UV_{max} 213 mμ (ε 8970).

XV: Colorless columns, mp 111.5—113°C. Found: C, 51.43; H, 5.16%; mol wt, 298. Calcd for $C_{12}H_{14}O_7\cdot \frac{1}{2}H_2O$: C, 51.61; H, 5.41%; mol wt, 279.24. UV_{max} 230 mμ (ε 7280). IR_{CHCl_3} 1630, 1700 cm^{-1}(C=C-C=O).

XXIV: Syrup, $[\alpha]_D^{22}$ +236.8° (*c* 0.641). Found: C, 52.53; H, 5.55%. Calcd for $C_{10}H_{12}O_6$: C, 52.63; H, 5.30%. UV_{max} 253 mμ (ε 6390). $IR_{fil\,m}$ 1640, 1705 cm^{-1} (C=C-C=O).

Reaction of XII with Hydrogen Bromide in Dry Benzene. A solution of XII (1.15 g) in dry benzene (21 m*l*) containing hydrogen bromide (2.34 g) was kept at 0—5°C for 1.5 hr. Evaporation of benzene under reduced pressure gave a dark red syrup, which was dissolved in methanol (8.4 m*l*) containing silver carbonate (1.53 g) and kept overnight at room temperature. The solution was filtered and evaporation of the filtrate gave a brown syrup. From the syrup, XX, XXI and XXII were isolated by preparative thin-layer chromatography (solvent B, R_f, 0.71 (XX), 0.93 (XXI), 0.85 (XXII), extracted with chloroform). Isolated materials were further purified by recrystallization or by preparative thin-layer chromatography.

XX: Syrup (purified by repeated preparative thin-layer chromatography, solvent D, R_f 0.50, yield, 0.1 g), $[\alpha]_D^{22}$ +66.6° (*c* 0.695). Found: C, 52.90; H, 5.97%. Calcd for $C_9H_{12}O_5$: C, 53.99; H, 6.04%. UV_{max} 226 mμ (ε 6800). $IR_{fil\,m}$ 1635, 1690 cm^{-1} (C=C-C=O).

XXI: Colorless columns, mp 136—138°C (recrystallized from ether and petroleum ether, yield, 10 mg), $[\alpha]_D^{22}$ −30.9° (*c* 1.045). Found: C, 40.88; H, 5.01; Br, 20.93%. Calcd for $C_{18}H_{19}O_8$ Br: C, 40.74; H, 5.00; Br, 20.86%.

41) Products isolated from the reaction were rather unstable and should be stored in a refrigerator under strictly anhydrous conditions.

XXII:[42] Syrup (purified by repeated preparative thin-layer chromatography, solvent B, R_f 0.85, yield, 0.03 g), $[\alpha]_D^{23}$ +51.3° (*c* 0.825). Found: C, 41.42; H, 5.10; Br, 20.82%. Calcd for $C_{13}H_{19}O_8$ Br: C, 40.74; H, 5.00; Br, 20.86%.

Reaction of V with Hydrogen Bromide in Dry Benzene. When the above reaction was carried out by using V as the starting material, the same result was obtained.

Conversion of XXII into XXI. When the above reaction was carried out by using XXII as the starting material (instead of hydrogen bromide, hydrogen chloride was used), the formation of XXI was confirmed by thin-layer chromatography.

Acid-catalyzed Isomerization of XII. A solution of XII (0.25 g) in acetic anhydride (3 m*l*) containing 1% of TsOH was kept at 40—50°C for 7 hr. When the solution was worked up in a way similar to the acid-catalyzed isomerization of V, a crude syrup (0.18 g) was obtained from which XIV (38 mg) and XV (15 mg) were obtainable.

Acid-catalyzed Isomerization of XIV. A solution of XIV (15 mg) in acetic anhydride (0.3 m*l*) containing 1% of TsOH was kept at 50°C for 8 hr. The formation of XV was confirmed by thin-layer chromatography (solvent F, R_f 0.40).

Isomerization of V in Acetic Acid. (i) A solution of V (2.0 g) in acetic acid-water (1: 1, v/v) was kept at 95°C for 4.5 hr. The syrup obtained on solvent removal under reduced pressure was purified by repeated preparative thin-layer chromatography (solvent D, R_f 0.70). XXVIb (0.36 g) was obtained and was identical to an authentic sample.[43] (ii) A solution of V (0.54 g) in acetic acid was kept at 95°C for 6 hr. The solution was worked up in a way similar to the above. XXVIb (0.07 g) was obtained. 2,4-Dinitrophenylhydrazone of XXVIb was prepared in a usual way as red needles, mp 142.5—147°C (recrystallized from ethanol). Found: C, 48.42; H, 3.57; N, 15.89%, mol wt, 357. Calcd for $C_{14}H_{17}O_7N_4$: C, 48.28; H, 3.47; N, 16.09%; mol wt, 348.27.

Isomerization of XII in Acetic Acid. A solution of XII (0.13 g) in acetic acid-water (1: 1, v/v) (2 m*l*) was kept at 95°C for 2 hr. A syrup was obtained on solvent removal under reduced pressure. From the syrup, traces of XXVIb were isolated by repeated thin-layer chromatography (solvent D, R_f 0.70 and solvent C, R_f 0.28).

Isomerization of XX in Acetic Acid. A solution of XX (40 mg) in acetic acid-water (1: 1, v/v) (1.5 m*l*) was kept at 95°C for 6 hr. Evaporation of the solvent gave a syrup (20 mg), the thin-layer chromatography of which indicated XXVIb as a major component and XX as a minor one (the ratio was about 2: 1).

The authors wish to express their deep gratitude to Dr. Ken'ichi Takeda, Director of this Laboratory, for his encouragement.

42) The NMR data show that the favorable conformation of XXII is Cl chair form.

43) Synthesized by Schubert's method. H. Schubert, E. Hagen and G. Lehrmann, *J. Prakt.*, **17**, 173 (1962).